The SOCMA Sulfosuccinates Group

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May 31, 2002

RETURN RECEIPT REQUESTED VIA E-MAIL

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Attn: Chemical Right-to-Know Program; HPV Reference Number:

Dear Administrator Whitman:

The SOCMA Sulfosuccinates Group is pleased to respond to the comments posted on the HPV web site, regarding our test plan. We have updated the test plan and robust summaries, and have included them for posting on the web site. There is also a separate document that outlines our response to the comments. If you or your staff have any questions, please feel free to contact me.

Sincerely,

James Cooper
Executive Director

cc: The SOCMA Sulfosuccinates Group Members

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May 29, 2002

Response to Comments by the EPA for the Sulfosuccinates Category

The EPA has reviewed the Sulfosuccinates Category Test Plan and provided comments relating to category justification, sufficiency of physicochemical and environmental data, health endpoints, ecotoxicity and robustness of selected summaries. In response to these comments the SOCMA Sulfosuccinates Group (SSG) has revised both the summary sets and the test plan as suggested and adds the following discussion:

Category Justification

The SSG believes that the data presented clearly demonstrate the justification for the Sulfosuccinates Category. Contrary to the comments of Environmental Defense, the SSG never stated that the members of the proposed class possess "identical functional groups." If that were the case, a single chemical, and not a category would have been presented. The SSG clearly points out that the single difference between each category member lies in the alkyl groups that form the alcohol moiety of the ester function. The category justification is demonstrated by the close similarity of the molecular structure of all category members, their similar physicochemical properties and the general consistency in values for most environmental and mammalian toxicity endpoints.

When administered by the oral route, the ethylhexyl ester can be eliminated unchanged or absorbed and metabolized by mammals. Available data suggest that the comparative degree to which elimination, versus absorption/metabolism, occurs varies in different mammalian species. The most likely route of metabolism is through esterase catalyzed de-esterification, as documented by the identification of 2-ethylhexanol or 2-ethylhexanol-forming compounds in the metabolism studies presented. Rapid esterase-catalyzed metabolism of aliphatic esters to the corresponding alcohols (e.g., for butyl acetate) is well documented. Whereas de-esterification of sodium diethylhexyl sulfosuccinate gives rise to 2-ethylhexanol, similar metabolism of sodium dicyclohexyl sulfosuccinate leads to the formation of cyclohexanol. Likewise, metabolism of sodium 1,3-dimethylbutyl sulfosuccinate leads to methyl isobutyl carbinol.

It is beyond the scope of this screening program to determine comparative degrees of excretion, versus absorption/metabolism, or to fully characterize the biological levels of metabolites for the category members. However, the discussion of currently available data on metabolism has been expanded to include a discussion of the alcohols formed from esterase-mediated metabolism of the cyclohexyl and dimethylbutyl esters. Genetic and developmental toxicity information about these metabolites (if available) has been added to the appropriate sections.

EPIWIN Modeling

The EPA correctly pointed out that for two category members (CAS No. 577-11-7 and 2373-38-8), the EPIWIN Program has an internal error of not assigning the correct SMILES codes to these CAS numbers. The SMILES codes assigned are for the corresponding sulfonic acids, and not for the sodium salts. For these two members the SSG has rerun the programs inputting the proper SMILES code for the sodium salts instead of inputting the CAS numbers. The SMILES codes are: CCCCC(CC)COC(=O)CC(C(=O)OCC(CC)CCCC) S(=O)(=O)O[Na] for CAS No. 577-11-7, and CC(C)CC(C)OC(=O)C(S(=O)(=O)O[Na])CC(=O) OC(C)CC(C)C for CAS No. 2373-38-8]. Some resulting physicochemical and environmental fate values were significantly changed, and others changed only slightly or not at all. The summary sets, test plan tables and test plan discussion have been revised to include the corrected values.

Physicochemical and environmental fate data

The EPA expressed a view that measured melting point data needs to be provided for all three category members. Measured values for the melting points of neat CAS Nos. 577-11-7 and 23386-52-9 have been added. The other category member is sold commercially as a mixture with water or with water plus either isopropyl alcohol or ethanol. As such this product is a liquid and does not correlate to a melting point for the hypothetical pure material. Measured water solubility data have been provided for all three category members. Measured boiling point and vapor pressure data do not apply to organic salts, since such salts tend to exist in ionic, not molecular form, and therefore do not volatilize significantly. The SSG believes that adequate data have already been provided to characterize the physicochemical properties of the category members at the screening level.

Ecotoxicity

The EPA recommends that an algal toxicity study be run on CAS No. 577-11-7, based on its higher lipophilicity relative to the other category members, and its significant toxicity toward fish and daphnia. We do not believe such a test is necessary. As mentioned, the ethylhexyl ester appears to be approximately 10-fold more toxic to fish and daphnia than the other esters (see Table 1 below). It is also approximately 10-fold more toxic to terrestrial plants. If it acts by a similar mechanism in algae, it would be reasonable to assume that it would be approximately 10-fold more toxic to algae than the dicyclohexyl ester.

As shown in the test with the dicyclohexyl ester, maximum stimulation of algal growth is observed at 8.1 to 90 mg/l. At higher concentrations, the stimulatory effect decreases (at 1000 mg/l the growth rate is essentially equal to control). Based on results with other surfactants, it is likely that concentrations higher than 1000 mg/l would be toxic. The effect of stimulation at low concentrations is likely due to the action of the surfactant on the algal membrane - at lower concentrations the membrane is disrupted only to the point

Table 1. Ecotoxicity data for Sulfosuccinates Category

Endpoint		Cyclohexyl ester, (CAS # 23386-52-9) (mg/l)	Dimethylbutyl ester, (CAS # 2373-38-8) (mg/l)	Ethylhexyl ester, (CAS # 577-11-7) (mg/l)
Acute toxicity to fish	Study	96 hr LC_{50} (bluegill) = 470	96 hr LC_{50} (bluegill, trout) > 1000; 1200	96 hr LC_{50} (bluegill, trout) = 37 ; 28
	ECOSAR	96 hr $_{LC50}$ =78 .2	96 hr LC_{50}=71.6	96 hr LC_{50}=6.09
Acute toxicity to Daphnia	Study	48 hr EC_{50} = 457	ND	48 hr EC_{50} = 36.2 mg/l
	ECOSAR	48 hr EC_{50} 505	48 hr EC_{50} = 431	48 hr EC_{50} = 5.94
Toxicity to algae	Study	No EC_{50} determined – Growth stimulated	ND	ND
	ECOSAR	96 hr EC_{50} 6.17	96 hr EC_{50} = 5.67	96 hr EC_{50} = .521

that permeability to nutrients is increased. However, at higher concentrations the membrane will become too porous and will result in cell lysis. This is likely to occur with all the members of the category, and is likely to be their mechanism of toxicity in animal and plant cells. Since the ethylhexyl ester has been shown to be approximately 10-fold more toxic in fish, daphnia and terrestrial plants than the others, it is reasonable to assume that it will be approximately 10-fold more potent than the cyclohexyl ester in causing stimulation, then inhibition of growth of algae. Based on this assumption, the concentrations of ethylhexyl ester likely to cause stimulation, and then inhibition of algal growth are up to 100 mg/l, and > 100 mg/l, respectively. We believe that such an estimation is reasonable, and obviates the need for testing. These statements have been added to the test plan.

Developmental toxicity

The EPA suggests the SSG needs to provide additional information on the toxicological and metabolic similarities of these chemicals to justify extrapolating general toxicity and developmental toxicity of sodium diethylhexyl sulfosuccinate to the other chemicals, or conduct these studies on one of them to characterize these endpoints.

The Group agrees with EPA that additional information can and should be given, particularly in regard to developmental toxicity. For this reason, more details and explanation have been added to the test plan with regard to metabolism with the developmental toxicity endpoint in mind.

An adequate developmental toxicity study has been summarized for sodium diethylhexyl sulfosuccinate. The metabolite 2-ethylhexanol has been extensively studied and reviewed in the OECD/SIDS program. Contrary to the EPA comments, the Sulfosuccinates Group did not state in Section 2.3 of the Test Plan that 2-ethylhexanol is a developmental toxicant. 2-Ethylhexanol has been shown not to exhibit developmental toxicity except at high doses that are maternally toxic. Cyclohexanol is currently under review and methyl isobutyl carbinol is slated for review as a high production volume

chemical. The data being presented in these reviews are available for those interested in further information regarding the developmental toxicity of these metabolites.

The general knowledge that aliphatic esters are readily metabolized to the alcohols lends further support to the category justification for mammalian endpoints. The demonstrated lack of significant developmental toxicity of these metabolites, including 2-ethylhexanol, as well as the low developmental toxicity of sodium diethylhexyl sulfosuccinate itself, should be sufficient for screening purposes, without conducting additional developmental toxicity studies.

Genetic toxicity

Text has been added that describes the overall lack of genetic toxicity of the potential alcohols that may be formed by the metabolism of the three different esters.

Reproductive toxicity

The fact that food consumption in the 90-day study for the 2-ethyl hexyl ester was not reduced is a point well-taken. The point that has been shown in the reproductive study with the ethylhexyl ester is that either the taste of the milk or the ability of dams to produce milk was reduced by the 2-ethylhexyl ester. Contrary to what was stated, there does not appear to be an affect on taste of the feed, since food consumption was not reduced in the 90-day study. Statements alluding to this concept have been removed.

Robustness of Summaries

Some study details were not originally provided for toxicity studies. The summaries have been revised to include the suggested corrections and details (if available) from the original studies, with the following exception:

In the reproductive toxicity studies, the weight of each litter was not determined. Therefore, it cannot be provided. A list of individual pup weights at termination is not necessary (and is therefore not provided). Over 4800 values would have to be entered. The summaries now include ranges for mean weights and other numerical values for treatment-related responses.

Other

The point by Environmental Defense that these sulfosuccinates have a high rate of use (and should therefore be scrutinized) is based on statements made in the test plan about the ethylhexyl ester (dioctyl sodium sulfosuccinate). Use information for the other sulfosuccinates was not listed in the original test plan. We have added this information to the revised test plan. One can conclude from this text that use of the dicyclohexyl and dimethylbutyl esters is not as widespread as the ethylhexyl ester.